Remarks/Arguments

Claims 39-46 and 49-51 are presently pending in this application and are rejected on various grounds. Claims 39-41 have been canceled without prejudice or disclaimer to pursue their subject matter in further continuing applications. The Examiner had not entered the previous amendments and indicated that the claims required additional corrections for grammatical errors. Applicants have amended claims to more clearly claim what the Applicant considers is the invention. The foregoing amendments to the claims are of formal nature, and do not add new matter; their entry is respectfully requested. Rejections to the pending claims are respectfully traversed.

Claim Rejections - 35 USC § 101 and 112, first paragraph

Claims 39-46 and 49-51 remain rejected under 35 U.S.C. §101 and 35 U.S.C. §112, first paragraph for lack of utility.

The Examiner asserts that "the rejection is made for lack of a specific and substantial utility that does not require further experimentation to identify a real world use for the claimed invention." Even though the Examiner acknowledges that "the exhibits (previously presented) clearly demonstrates that (the) injection of PRO302 protein intra-dermally in guinea pigs will cause some vascular leakage," the Examiner says that "there is no convincing evidence or rational that PRO302 plays any role whatsoever in vascular leakage in its usual role(s) *in vivo*." The Examiner adds "there is no convincing evidence or argument for a specific role for PRO302 in any condition that involves vascular integrity (e.g. pulmonary leakage, capillary leakage, tumor leakage or burns). Applicants respectfully traverse the rejection.

Utility Standard for "specific and substantial"

Under the Utility Guidelines, a utility is "specific" when it is particular to the subject matter claimed. For example, it is generally not enough to state that a nucleic acid is useful as a diagnostic without also identifying the conditions that is to be diagnosed.

The requirement of "substantial utility" defines a "real world" use, and derives from the Supreme Court's holding in *Brenner v. Manson*, 383 U.S. 519, 534 (1966) stating that "The basic *quid pro quo* contemplated by the Constitution and the Congress for granting a patent monopoly

is the benefit derived by the public from an invention with substantial utility." In explaining the "substantial utility" standard, M.P.E.P. 2107.01 cautions, however, that Office personnel must be careful not to interpret the phrase "immediate benefit to the public" or similar formulations used in certain court decisions to mean that products or services based on the claimed invention must be "currently available" to the public in order to satisfy the utility requirement. "Rather, any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient, at least with regard to defining a "substantial" utility." (M.P.E.P. 2107.01, emphasis added.) Indeed, the Guidelines for Examination of Applications for Compliance with the Utility Requirement, set forth in M.P.E.P, 2107 II (B) (1) gives the following instruction to patent examiners: **"If the (A)pplicant has asserted that the claimed invention is useful for any particular practical purpose . . . and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility."**

Arguments

Based on the positive results obtained in the vascular permeability assay, which the Examiner has acknowledged as true based on the evidence presented as exhibits with the previous response, Applicants had asserted a **specific and substantial** role for PRO302 where vascular leakage occurs like in pulmonary leakage, capillary leakage, tumor leakage or burns. Yet, the Examiner maintains this rejection. Without acquiescing to the propriety of this rejection, merely to expedite prosecution in this case, Applicants will file an executed Declaration by Sherman Fong, Ph.D., an expert in the field of immunology, with discussions on the vascular leakage assay and how this assay identifies molecules that induce leakage, the mechanism of vascular leakage/permeability, how the assay and its modifications have been widely used in the art by several investigators in the identification of various well-established leak inducing molecules like VEGF (VPF) etc. and specific uses. Specific utilities for the PRO302 molecule and how such utilities would readily be understood and accepted as credible, substantial and specific, by those skilled in the art, which will also be discussed by Dr. Fong in his declaration.

Accordingly, Applicants believe that one skilled in the art would know how to make and use the present invention based on the Applicants' disclosure and thus, the present rejection under 35 U.S.C. §101 and §112, first paragraph should be withdrawn.

Claim Rejections - 35 USC 112, first paragraph- Written description

Claims 39-44, 47-48, 50-51 remain rejected under 35 U.S.C. §112, first paragraph for lack of showing of possession of the claimed invention.

Without acquiescing to the propriety of this rejection, merely to expedite prosecution in this case, Applicants have canceled claims 39-41 without prejudice or disclaimer and hence, this rejection is moot for these claims.

Further, Example 14 of the Written Description Guidelines issued by the U.S. Patent Office which clearly states that "protein variants meets the requirements of 35 U.S.C.§112, first paragraph as providing adequate written description for the claimed invention even if the specification contemplates but does not exemplify variants of the protein if (1) the procedures for making such variant proteins is routine in the art, (2) the specification provides an assay for detecting the functional activity of the protein and (3) the variant proteins possess the specified functional activity and at least 95% sequence identity to the reference sequence". Based on these guidelines, Applicants submit that the instant specification evidences the actual reduction to practice of a full-length native human PRO302 polypeptide of SEQ ID NO: 255, with or without its signal sequence and of the nucleic acid of SEQ ID NO: 254. In addition, the specification provides detailed description about the cloning of variants and describes the gene amplification assay for testing nucleic acids in a PCR based assay. Thus, Applicants submit that the genus of polypeptides of SEQ ID NO: 255 or its variants with 95% identity, further possessing the functional property of "enhancing vascular permeability," would encompass a genus that meets the requirements of 35 U.S. C. §112, first paragraph as providing adequate written description.

Thus, one of skill in the art would know that Applicants had possession of the invention, as described in the instantly amended claims, and therefore request that this rejection be withdrawn.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 08-1641 (Attorney Docket No.: 39780-1618P2C39). Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

Date: December 14, 2004

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